

**AMENDMENTS TO THE DRAWINGS**

Submitted herewith please find four (4) sheets of replacement drawings in compliance with 37 C.F.R. § 1.84. The Examiner is respectfully requested to acknowledge receipt of these drawings.

The submitted replacement drawings are intended to replace the drawings previously submitted.

Enclosure: Replacement Drawings: 4 sheets (Figs. 2-5)

**REMARKS**

In the present Amendment, claim 28 has been amended to correct “A” to --The--. New claims 34 and 35 have been added. Support for claims 34 and 35 is found, for example, at page 32, line 26 of the specification. Replacement drawings (Figs. 2-5) with correct legends are being submitted. Support is found, for example, in Test Examples 4 and 5 at pages 52 and 53 of the specification. No new matter has been added, and entry of the Amendment is respectfully requested.

Upon entry of the Amendment, claims 1-35 will be pending, of which claims 1-20, 31 and 32 are withdrawn from consideration.

At page 2 of the Action, claims 21-24, 28-30 and 33 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Akiyama et al. (US 5,593,690, “Akiyama”) in view of British Plastics and Rubber (2001) as evidenced by Lochtec ApS.

At page 7 of the Action, claims 25-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Akiyama and British Plastics and Rubber, and further in view of Kojima et al. (J. of Controlled Release, 2002, “Kojima”).

Applicant submits that the above two rejections should be withdrawn because the cited references do not disclose or render obvious the present invention, either alone or in combination.

Akiyama discloses that “the coating may be carried out by, for example, spraying a liquid made by dispersing or dissolving the coating agent in water or an organic solvent” (col. 6, line 65 - col. 7, line 2). Akiyama also discloses in Examples 23 and 24 spraying an aqueous solution of hydroxypropylmethylcellulose using a fluid-bed drier to form a coating.

However, Akiyama nowhere teaches or suggests the fusion coating of the present invention (as disclosed at page 37, lines 3 to 12 of the specification). This point is also acknowledged by the Examiner.

The Examiner states that British Plastic Rubber (2001) discloses Cyclomix 5 as a mixer, and that the details of Cyclomix 5 are shown in Lochtec ApS. However, in spite of the fact that British Plastic Rubber (2001) is originally a published document, its abstract available online (website: [www.highbeam.com/doc/1G1-7091211.html](http://www.highbeam.com/doc/1G1-7091211.html)) is listed in the Notice of References Cited attached to the Office Action. The Examiner has not confirmed whether the original document for British Plastic Rubber (2001) has the same content as the abstract on the website.

Accordingly, BPR is not a legally effective prior art document.

Furthermore, although Vrieco-Nauta<sup>TM</sup> Cyclomix 5 High Intensity Mixer described on page 5 of Lochtec ApS has heating and cooling functions, LochtecApS also discloses that “[t]he design ... prevents material fusion.” This indicates that Cyclomix 5 precludes fusion of coating particles. That is, Lochtec ApS strongly teaches away from fusion-coating, which is employed in the present invention.

As explained above, Akiyama nowhere teaches fusion coating, and Cyclomix 5 disclosed in British Plastic Rubber (2001) in view of Lochtec ApS teaches away from fusion-coating. Accordingly, the fusion coating of the present invention would not have been obvious to a person skilled in the art from the combination of Akiyama and British Plastic Rubber (2001) in view of Lochtec ApS.

Further, in the present invention, the inventor focused on problems during fusion coating, such as the occurrence of electrostatic adhesion of core particles, and mainly focused on solving these problems. There is no recognition of such problems in any of the cited references.

Although a polyglycerol fatty acid ester is mentioned as one of the various examples in Akiyama, a person skilled in the art would never select, with an expectation of success, a matrix base material having a specific hydroxyl value (a polyglycerol fatty acid ester), without recognizing the problems during fusion coating.

Still further, as explained in the previous Amendment, a characteristic feature of the present invention is fusion coating by agitation (agitation granulation method). This method can achieve two remarkable effects: inhibition of adhesion of core particles to the wall surface of a granulator during fusion coating; and production of particles of a matrix formulation having stable drug release control properties.

Refer to, for example, the following paragraph at page 38, lines 11 to 27 of the specification.

In **fluid beds**, to heat core particles to a temperature near their melting point, hot air having a temperature higher than the melting point is necessary, and because of the high temperature of the fluid-bed apparatus (side walls, meshed portion at the bottom, etc.) the core particles fuse, adhere to the apparatus, and cluster, resulting in impaired yields. Moreover, it is sometimes practically impossible to tightly and completely affix powder to the core particles for the purpose of sustained medicament release. In contrast, when **agitation method** is employed, the container temperature (jacket temperature) of the mixer can be desirably controlled to a temperature substantially identical to the temperature of the core particles. Moreover, the entire apparatus can be rapidly cooled by introducing cold water into the jacket. Therefore, the core particles are barely overheated, completely preventing the core particles from aggregating due to fusion and adhesion to sidewalls."

Specifically, Test Example 5 and Fig. 5 show that particles fusion-coated by the agitation method are highly effective in controlling elution of the drug, compared to particles fusion-coated by the fluid-bed method. That is, particles produced by the agitation method are excellent in terms of drug release control (has a novel property), compared to particles produced by the fluid-bed method.

Such remarkable effects cannot be expected from the disclosure of Akiyama, which is silent as to fusion coating, or from British Plastic Rubber (2001), which teaches away from fusion of the material.

Accordingly, the present invention is unobvious and is patentable over the combination of Akiyama and British Plastic Rubber.

Kojima is cited as teaching that the release rate of theophylline was decreased by annealing at 80 °C for 4 h and that annealing of the matrix particles leads to alterations of the pellet structure and, consequently, of the release properties (page 339, 1st column, 1st full paragraph). Kojima does not make up for the deficiencies of Akiyama and British Plastic Rubber.

In view of the above, reconsideration and withdrawal of all the §103(a) rejections based on the cited references are respectfully requested.

Allowance is respectfully requested. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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WASHINGTON OFFICE

**23373**

CUSTOMER NUMBER

/Hui C. Wauters/  
Hui C. Wauters  
Registration No. 57,426

Date: September 1, 2011

**PATENT APPLICATION**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of

Docket No: Q92094

Yuso TOMOHIRA

Appln. No.: 10/561,444

Group Art Unit: 1612

Confirmation No.: 6406

Examiner: Darryl C SUTTON

Filed: December 20, 2005

For: MEDICAMENT SUSTAINED-RELEASE PARTICLES AND METHOD FOR PREPARING  
THE SAME

**EXCESS CLAIM FEE PAYMENT LETTER**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

An Amendment Under 37 C.F.R. § 1.114(c) is attached hereto for concurrent filing in the above-identified application. The resulting excess claim fee has been calculated as shown below:

	After Amendment		Highest No. Previously Paid For					
All Claims	<u>35</u>	-	<u>33</u>	=	<u>2</u>	X	<u>\$52.00</u>	= <u>\$104.00</u>
Independent	<u>5</u>	-	<u>5</u>	=	<u>0</u>	X	<u>\$220.00</u>	= <u>\$0</u>
<b>TOTAL</b>								<b>= <u>\$104.00</u></b>

The statutory fee of \$104.00 is being remitted. The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,  
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